Weights (IPCW), and Iterative Parameter Estimation (IPE). To determine acceptance of these techniques in Australia, Public Summary Documents (PSDs) reporting on the Pharmaceutical Benefits Advisory Committee's (PBAC's) decision-making in oncology were reviewed. **METHODS:** Oncology PSDs were examined, and the method of adjustment (if any), PBAC concerns and outcome were assessed. **RESULTS:** Thirty-one submissions included trials allowing crossover; 16 (52%) presented adjusted estimates of OS. Common indications were: renal cell carcinoma, non-small cell lung cancer (NSCLC), melanoma, colorectal cancer (CRC), and pancreatic neuroendocrine tumour. The most common method was RPSFT (11 products), followed by IPCW (4 products). IPE, marginal structural modelling, and a two-stage Weibull approach were each reported once. The RPSFT approach appeared to raise fewer concerns than the IPCW, usually because the IPCW correction was considered less reliable when a high proportion of patients crossed-over. In NSCLC and CRC, the PBAC considered unadjusted crossover to be appropriate and reflect a relevant comparison between first- and second-line therapy. Only five PSDs reported results of more than one method. The PBAC expressed a preference to see a range of approaches and a clearly justified selection of the most appropriate method. **CONCLUSIONS:** A range of adjustment techniques were used to support submissions in Australia, with RPSFT being most common. It is important to clearly justify the need for adjustment and the selection of the most appropriate technique.

PCN60

SAFETY AND INSURANCE PREMIUM IMPLICATIONS FOR HOSPITALS BASED ON SUBCUTANEOUS VERSUS INTRAVENOUS ADMINISTRATION OF ONCOLOGY / HEMATOLOGY THERAPIES: CASE STUDIES WITH RITUXIMAB (MABTHERA) AND TRASTUZUMAB (HERCEPTIN)

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OBJECTIVES: In oncology an important parameter of safety is the potential treatment error in hospitals. The hypothesis which is being analyzed in the underlying work is the potential benefit of hospitals from a safety reduction through fix-dose ready to use subcutaneous therapies in comparison to intravenous therapies with trastuzumab and rituximab. **METHODS:** For the calculation of risk levels the Failure Mode and Effect Analysis (FMEA) approach was being applied. Within that approach the critical treatment path is followed and risk classification for each individual step is being estimated. For the oncology and hematology administration there were 35 different risk steps assessed. The study was executed in 17 hematology and 16 breast cancer centers in Italy. **RESULTS:** When the risk classes are calculated there were eight high risk areas identified for the administration of an intravenous therapy in hematology or oncology, 13 areas would be defined as having a median risk and 14 areas as having a low risk classification (total risk areas: n=35). When the new subcutaneous formulation would be applied 23 different risk levels could be completely eliminated (65% reduction). Including those eliminations important high risk classes such as the following were included: dose calculation, preparation and package labeling, preparation of the access to the vene and pump infusion preparation and infusion monitoring. The overall risk level for the intravenous administration was estimated to be 756 (ex-ante) and could be significantly reduced by 70% (ex-post). The potential harm compensation for errors related to the pharmacy would be decreased from 234'271 € for eight risk classes to only 3 risk classes. **CONCLUSIONS:** The use of a subcutaneous administration of trastuzumab (breast cancer) and rituximab (hematology) might lower the risk of administration and treatment errors for patients and could hence indirectly have a positive financial impact for hospitals.

PCN61

ASSOCIATIONS OF METFORMIN USE WITH MORTALITY AND DISEASE PROGRESSION AFTER CURATIVE HEPATIC RESECTION IN HEPATOCELLULAR CARCINOMA WITH TYPE 2 DIABETES MELLITUS: A NATIONWIDE POPULATION-BASED STUDY

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OBJECTIVES: There is a paucity of study to examine the relationship between metformin use and hepatocellular carcinoma (HCC) specific survival or recurrence. We, therefore, conducted a nationwide population-based study in the patients with HCC who underwent curative resection to investigate whether metformin use would reduce mortality and recurrence rate. **METHODS:** The study population initially included 105,367 adults who had a primary diagnosis of HCC (International Classification of Diseases, 10th revision, C22) from the Korea Center Cancer Registry between 1 January 2005 and 31 December 2011. The primary outcome was HCC-specific survival. We obtained HCC deaths from the National Population Registry of the Korea National Statistical Office through December 31, 2013, with the use of a unique personal identification number. The secondary outcome was tumor recurrence during follow-up periods from National Health Insurance Service. **RESULTS:** The HCC-related survival or recurrence-free was significantly higher in the metformin user group than in the metformin non-user group during the follow-up period. In unadjusted analyses, compared to non-metformin group, metformin group showed a significant lower risk of HCC-specific death (hazard ratio (HR), 0.40; 95% Confidence interval (CI), 0.32-0.51). After multivariable adjustments for clinical covariates, metformin group still had a significantly lower risk of events as compared with non-metformin group (HR, 0.38; 95% CI, 0.30-0.49). The adjusted risk for recurrence was also significantly lower in metformin group (HR, 0.41; 95% CI, 0.33-0.52) compared with that of non-metformin group. **CONCLUSIONS:** Among patients of HCC cohort treated with curative hepatic resection, metformin use was associated with improvement of HCC-specific mortality and recurrence risk.

PCN62

IMPROVED SURVIVAL WITH IPILIMUMAB IN PATIENTS WITH ADVANCED MELANOMA IN REAL-WORLD CLINICAL PRACTICE: FIRST RESULTS OF THE DUTCH MELANOMA TREATMENT REGISTRY

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OBJECTIVES: Ipilimumab improved the survival of advanced melanoma patients in phase III trials (MDX010-20 [previously treated patients] and CA184-024 [treatment naïve patients]). Uncertainty exists, however, whether this benefit can be translated to real-world clinical practice. We investigated the use and survival outcomes of ipilimumab in The Netherlands. **METHODS:** We retrieved data from the population-based Dutch Melanoma Treatment Registry (DMTR). The DMTR includes all Dutch patients with unresectable stage IIIc/IV melanoma. Detailed data were prospectively collected from start of diagnosis until death or loss to follow-up. Survival outcomes (overall survival [OS] and one-year survival) in patients receiving ipilimumab in clinical practice were assessed using Kaplan-Meier estimates, and were compared with outcomes of pivotal trials and outcomes of real-world patients diagnosed before the introduction of ipilimumab (2003-2011; stage IV only) using data from the Dutch Comprehensive Cancer Centres. **RESULTS:** From 2012-2015, 545 patients received at least one dose of ipilimumab in real-world practice (65% received four dosages; median follow-up 4.6 months; data cut-off March 9, 2015). Ipilimumab was most frequently prescribed in the second line (60%), followed by the first (31%), third (8%), and fourth line (2%), respectively. Median OS was 7.7 months (IQR:3.6-NR) and one-year survival was 40%. This is somewhat lower than in the pivotal trials, which may be due to differences in baseline characteristics and time of follow-up (MDX010-20: median follow-up 27.8 months, median OS 10.1 months, one-year survival 46%; CA184-024: median follow-up 11.0 months, median OS 11.2 months, one-year survival 48%). However, the survival was higher compared to the survival in the period before the introduction of ipilimumab (2003-2011: median OS 6.8 months [IQR:3.3-18.5], one-year survival 33%). **CONCLUSIONS:** Melanoma survival has improved since the introduction of ipilimumab. Although survival was somewhat lower in real-world compared to pivotal trials, a survival benefit was observed in Dutch real-world clinical practice.

PCN63

WHEN "ALIVE AFTER 5 YEARS" DOES NOT MEAN "CURED": INTERNATIONAL PATTERNS IN CANCER 10- TO 20- YEAR RELATIVE SURVIVAL RATES

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OBJECTIVES: Traditionally, patients who survive 5 years from diagnosis of cancer are considered to be cured. More recent analysis of adjusted mortality rates suggests this assumption may not be valid. We sought to identify data on relative survival at 10 to 20 years for common cancers to determine which showed a continuing increase in mortality beyond 5 years. **METHODS:** National or regional cancer databases reporting net or relative survival beyond 5 years from diagnosis were identified, with 5- and 10-year data available from England and Wales, Scotland, the USA, Switzerland and Slovakia; 5-, 10- and 15-year data from Norway; and 5-, 10-, 15- and 20-year data from Germany and Sweden. The percentage decrease in net survival at each 5-year step was calculated at 10, 15 and 20 years to identify where there was a persistent increase in all-cause mortality above expected for the age- and sex-adjusted cancer-free population. **RESULTS:** Regional setting had a large impact on relative survival for each type of cancer. However, oropharyngeal, head and neck, liver, lung, pancreatic and ovarian cancers, chronic lymphocytic leukaemia, mesothelioma, multiple myeloma, and Kaposi's sarcoma consistently showed between a 10% and 70% further decrease in relative survival at 10 compared with 5 years. A further 10% or greater decrease in relative survival was seen between 10 and 20 years from diagnosis for head and neck, lung, laryngeal and prostate cancer, and was around 40% lower than population norms at 20 years for people with multiple myeloma. **CONCLUSIONS:** When modelling the impact of treatments for cancer, it is important to consider the whole period of increased risk of mortality. For certain cancers, in particular multiple myeloma, lung, prostate and laryngeal cancer, this may require a time horizon of 20 years or longer.

PCN64

IMPROVED SURVIVAL IN PATIENTS WITH ADVANCED MELANOMA IN REAL-WORLD CLINICAL PRACTICE: FIRST RESULTS OF THE DUTCH MELANOMA TREATMENT REGISTRY

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OBJECTIVES: New drugs for advanced melanoma showed promising results in pivotal trials; however, uncertainty exists regarding their value in real-world clinical practice. We investigated real-world treatment patterns and outcomes of advanced melanoma in The Netherlands. **METHODS:** We retrieved data from the population-based Dutch Melanoma Treatment Registry (DMTR). The DMTR includes all Dutch patients with unresectable stage IIIc/IV melanoma. Detailed data were prospectively collected from start of diagnosis until death or loss to follow-up. Real-world treatment patterns and outcomes (overall survival [OS], one-year survival and time-to-next-treatment [TTNT]) were assessed in patients receiving systemic treatment

using Kaplan-Meier estimates. Additional data from the Dutch Comprehensive Cancer Centres (stage IV only) were used to compare survival outcomes in two time periods (2003-2011 versus 2012-2015). **RESULTS:** From 2012-2015, 1259 patients received systemic treatment (median follow-up 12.6 months; data cut-off March 09, 2015). The most frequently prescribed treatments were ipilimumab (29%) and vemurafenib (29%), followed by trial-based treatments (27%), chemotherapy (11%), and dabrafenib (4%). Vemurafenib was the most frequently applied treatment in the first line (41%), ipilimumab in the second line (56%), and trial-based treatments in the third and fourth line (41% and 63%, respectively). The median TTNT was 5.4, 4.7 and 4.3 months in the first, second, and third line, respectively. The median OS was 9.6 months (IQR 4.6-18.6) and the one-year survival was 41% (unresectable stage IIIc [n=33]: median OS 32.8 months, one-year survival 71%; stage IV [n=1226]: median OS 9.3 months, one-year survival 40%). In contrast, survival outcomes of stage IV melanoma were much lower in the period before the introduction of new drugs (2003-2011: median OS 6.8 months, one-year OS 33%). **CONCLUSIONS:** Melanoma survival has improved since the introduction of new drugs for advanced melanoma. The survival gain shown in pivotal trials was also observed in real-world clinical practice in The Netherlands.

PCN65

MORTALITY TRENDS IN CANCERS: A NEW MODEL TO VISUALISE THE CONTRIBUTION OF SPECIFIC DISEASES, COHORTS AND CODING CHANGES TO OVERALL MORTALITY IMPROVEMENT

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OBJECTIVES: Identifying the drivers of trends in mortality for disease classes is challenging. We used the Requiem model to visualise trends by gender and age in 3-D format to identify cohort and other effects in specific cancers. **METHODS:** The Requiem model analysed and smoothed ONS mortality statistics for England and Wales from 1970 to 2013 by single year of age and gender. Disease codes were mapped at 4-digit level from ICD-8 to ICD-10 by medical modellers. An analysis was run for total cancer mortality and individual malignant diseases within that category. Outputs were displayed in multiple formats, including 3-D images of central mortality and deaths by age over time, and heat maps of absolute mortality improvement per disease and the component each disease contributed to all-cause mortality trends. **RESULTS:** Cancer mortality increased from 1970 to 1990s and has since fallen by up to 4% per year, accounting for a 1-2% of absolute improvement in all-cause mortality, and with evidence from heat maps for cohort effects. Most cancers showed increasing mortality rates to the 1990s, which have now declined. This is seen particularly in men in lung cancer, which saw up to 10% improvement per year in mortality, in breast cancer in women, with a peak in the 1980s and up to 20% annual improvement since then, and in colon cancer in both genders, with a 5-10% annual improvement in mortality per year. Hodgkin's lymphoma mortality has decreased steadily in both genders, while non-Hodgkin's mortality has increased in the over 50s. Mortality continues to worsen for liver, kidney and CNS cancers. Pancreatic cancer has shown little change in mortality since 1970 in either gender. **CONCLUSIONS:** The Requiem model 3-D visualisation facilitates the understanding of trends in mortality for different cancers, and shows the impact of cohort effects and risk factors such as smoking and alcohol.

PCN66

EVALUATION OF 'REAL-WORLD' IPILIMUMAB DATA IN IRELAND

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OBJECTIVES: Ipilimumab is licensed for the treatment of adults with advanced (unresectable or metastatic) malignant melanoma. It was approved for reimbursement in Ireland in 2012, through the Oncology Drug Management System (ODMS). The ODMS was introduced by the National Cancer Control programme in July 2012. The scheme allows direct hospital reimbursement for approved high cost anti-cancer drugs for individual patients. Drugs must be prescribed for approved indications according to license informed protocols. The online based system is designed to collect information from hospitals (26 nationally) in relation to patient demographic data, cancer drug use and spending. This data is maintained by the payer (Primary Care Reimbursement Service (PCRS)). The objective of this study is to examine this real world data of patients treated with ipilimumab. **METHODS:** The PCRS extracted data on all patients who had received ≥1 dose of ipilimumab (June 2012 - May 2015) in the public hospital setting through the ODMS. Patient data included patient demographics, the quantity of ipilimumab supplied and the reimbursement claim data. The National Centre for Pharmacoeconomics analysed this anonymised data. Kaplan-Meier survival curves were constructed using the Tierney et al methodology. Survival data was extrapolated using the Hoyle and Henley methodology. **RESULTS:** A total of 205 patients who had received ≥1 dose ipilimumab over the period of analysis were identified. The mean age of the cohort was 60.4 years (SD ±14) and 58.5% were male. All 4 cycles of ipilimumab were received by 59% of patients. Seven patients were re-treated with the drug. Empirical and extrapolated real world survival data were compared to clinical trial evidence. **CONCLUSIONS:** The analysis provides real world survival outcomes for patients with advanced malignant melanoma treated with ipilimumab in Ireland. Examination of this evidence is prudent in advance of the launch of the PD1 inhibitors for malignant melanoma.

PCN67

RETROSPECTIVE COMPARISON OF REAL-LIFE SURVIVAL DATA FROM SINGLE CENTRE TRIALS - THE CLINICAL OUTCOME OF VEMURAFENIB THERAPY IN METASTATIC MELANOMA PATIENTS

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OBJECTIVES: The selection of the MM patient group, eligible for BRAFi therapy is based on the molecular pathologic diagnostics of the BRAF V600 gain-of-function mutation. The sensitivity and specificity of Cobas 4800 BRAF V600 in vitro diagnostic test is excessively high to detect the V600 mutation. In the BRIM-3 study, vemurafenib showed improved PFS and OS in patients carrying BRAF mutation. Our aim is to analyze the vemurafenib international and local real-life survival data of the patients treated in the National Institute of Oncology, in case of individual reimbursement application. **METHODS:** We retrospectively assessed the single centre Hungarian real-life survival data from 2012 to May 2015. We compared the outcome of the Hungarian and the French real-life and BRIM-3 data. **RESULTS:** In the selection of the patient group suitable for BRAFi therapy, we carried out 277 BRAF mutation analysis with Cobas test during the given period. 148 cases were wide type, the mutation rate was 46,57% with 129 mutant cases. In Hungary, BRAFi therapy is reimbursed, only on the basis of individual reimbursement application. 36 MM patients were enrolled, with median age of 53,5 years. The median PFS reached 5,4 months, the OS reached 12,3 months. In the previously published French single centre trial, in temporary authorisation program, the median PFS was 3,6 months, the median OS was 7,5 months. The BRIM-3 study demonstrated mPFS 6,9 months and OS 13,6 months. **CONCLUSIONS:** The detection of BRAF mutation is essential in the therapeutic strategy of metastatic melanoma patients. The Cobas 4800 BRAF test allows a more exact selection of the patient group to be treated by BRAFi. Our single centre OS data are close to BRIM3 clinical trial data. In case of previous vemurafenib therapy started in appropriate treatment line, further improvement can be expected in survival results.

CANCER – Cost Studies

PCN68

THE BUDGET IMPACT OF DENOSUMAB IN THE TREATMENT OF GIANT CELL TUMOR OF THE BONE (GCTB) IN BELGIUM

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OBJECTIVES: To estimate the budget impact in Belgium of denosumab (120 mg) in the treatment of GCTB, an extremely rare, locally aggressive benign tumor often leading to severe destruction of bone and extension into the surrounding soft tissues. **METHODS:** A budget impact model was developed, combining epidemiological data, proportions of resectable and unresectable GCTB disease, and eligibility for treatment with denosumab. Evidence collected in clinical trials is used to estimate the denosumab clinical effect. Publicly available costs of the relevant surgical procedures and the actual cost for denosumab 120 mg from payer perspective are considered. The clinical effect of denosumab in delaying or downgrading invasive surgeries is estimated by comparing the surgical procedures planned at trial entry and the procedures actually performed during the trial. To calculate the savings in surgical procedures, the downgrade in planned procedures and only 50% of the avoided procedures in the trial period were considered. Resource use associated with the surgical procedures included the need for rehabilitation and re-hospitalizations due to complications. Savings were only applied to patients with resectable tumors. The model does not take into account the full clinical benefit of denosumab including decrease in disease progression in patients who have not undergone surgery. The time horizon considered was 3 years. **RESULTS:** Denosumab is expected to be provided to 32, 42 and 53 patients in year 1, 2 and 3, respectively. 550,940 euros of total drug expenditure are expected. Savings were estimated at 409,372 euros, the majority of which was attributable to fewer and less severesurgical procedures. The impact of denosumab on the overall health care budget is 141,568 euros over three years. **CONCLUSIONS:** The introduction of denosumab in the treatment of GCTB has a manageable budget impact in Belgium. Seventy four percent of the denosumab expenditure is off-set thanks to its clinical benefit.

PCN69

BUDGET IMPACT ANALYSIS OF DASATINIB AS A SECOND-LINE THERAPY IN PATIENTS WITH CHRONIC MYELOGENOUS LEUKEMIA (CML) IN THE RUSSIAN FEDERATION

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OBJECTIVES: CML is among seven nosologies included in the federal program for supply of medicines to patients with rare diseases in the Russian Federation. Currently only first-generation tyrosine kinase inhibitor - imatinib is available to CML patients within this program. However from 25% to 30% of CML patients in Russia have intolerance or develop resistance to imatinib and require second line therapy with dasatinib or nilotinib. **METHODS:** This study includes budget impact analysis (BIA) for dasatinib as a second-line CML therapy. Only direct pharmacotherapy costs were considered. Annual treatment cost of dasatinib amounts to 1,720,111 rubles (28,365 €) for chronic phase. Time horizon was set at 1 year. In the baseline scenario it was assumed that 100% of the imatinib-resistant patients are treated with high-dose imatinib in frame of the federal "seven nosologies" program. In the future scenario upon dasatinib inclusion into aforementioned program the percentage of patients that would be possible to switch from high-dose imatinib to dasatinib without increase of the total national CML budget was calculated. Also annual economic impact of providing dasatinib as a second-line therapy to 100% of the eligible patients was estimated. Assumptions regarding adherence to treatment of patients diagnosed with CML and actual medication consumption rate were included into analysis. **RESULTS:** Budget impact analysis was carried out for a total population of 7100 patients according to the national CML registry in 2015. Centralized purchase of dasatinib in frame of the federal program could save 463 mln rubles (7,7 mln €) or 10% of the actual total CML budget in Russia. **CONCLUSIONS:** With consideration for actual dasatinib use within regional drug provision programs it was demonstrated that 100% of the imatinib-resistant and intolerant patients can be provided with dasatinib